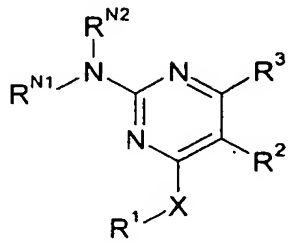
CLAIMS

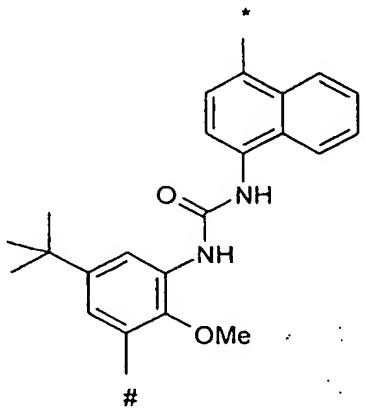
1. The use of a compound of formula I:



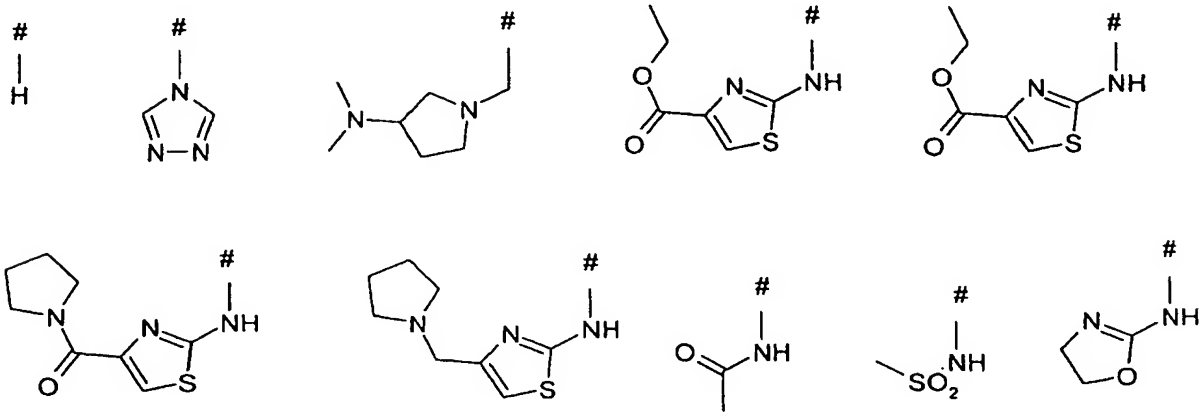
(I)

or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT_{2B} receptor,
wherein:
X is O or NH;
R^2 and R^3 are independently selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;
R^1 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;
R^{N1} and R^{N2} are either:
(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N3}R^{N4}$, where n is from 1 to 4 and R^{N3} and R^{N4} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or
(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group;
with the proviso that when R^2 is H, R^3 is H or Me, R^{N1} and R^{N2} are either (i) independently selected from H, R, R', $(CH_2)_nNR^{N3}R^{N4}$, where n is from 1 to 4 and R^{N3} and R^{N4} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted

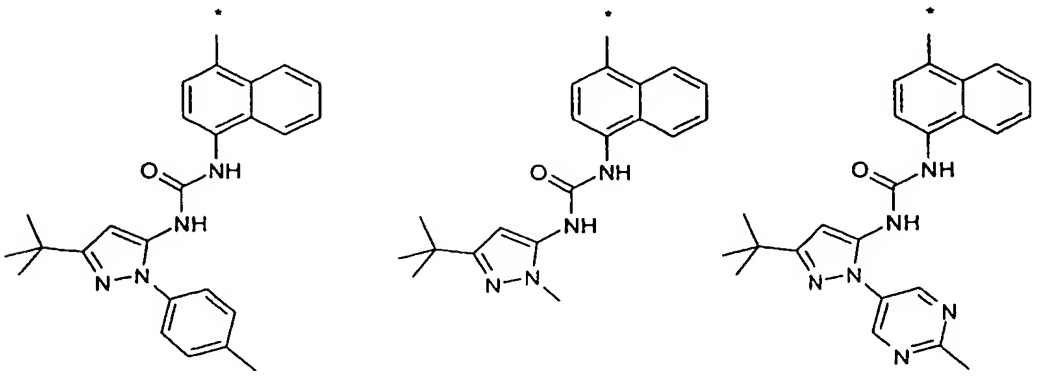
phenyl-C_{1-4} alkyl, or (ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-6} heterocyclic group; and X is O, then R^1 is not:



wherein # is:



and R^1 is not:



2. The use according to claim 1, wherein R^{N1} and R^{N2} are independently selected from H and R.

3. The use according to claim 2, wherein R^{N1} and R^{N2} are both H.

4. The use according to any one of claims 1 to 3, wherein R^2 is H.

5. The use according to any one of claims 1 to 4, wherein R^3 is methyl.

6. The use according to any one of claims 1 to 5, wherein X is NH.

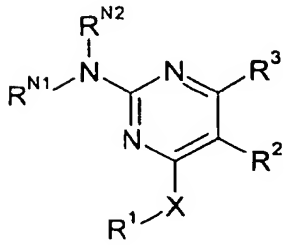
7. The use according to any one of claims 1 to 6, wherein R^1 is an optionally substituted naphthyl group.

8. The use according to any one of claims 1 to 6, wherein R^1 is an optionally substituted biphenyl group.

9. The use according to claim 1, wherein R^1 is an optionally substituted bi-C_{5-7} aryl group or a C_{9-14} aryl group optionally substituted with substituent groups independently selected from the group consisting of C_{1-4} alkyl, halo, hydroxy, alkoxy, cyano, amino and amido.

10. The use according to any one of claims 1 to 9, wherein the condition alleviated by antagonism of a 5-HT_{2B} receptor is a disorder of the GI tract.

11. A compound of formula I:



(I)

or a pharmaceutically acceptable salt thereof for use in a method of therapy, wherein:

X is O or NH;

R^2 and R^3 are independently selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;

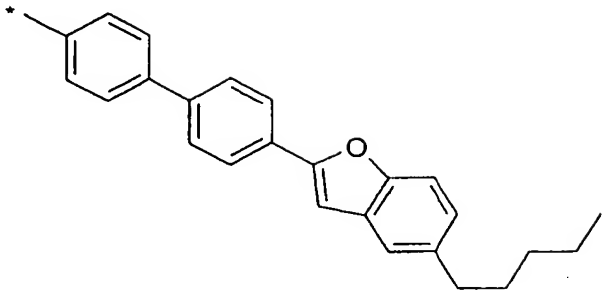
R^1 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N1} and R^{N2} are either:

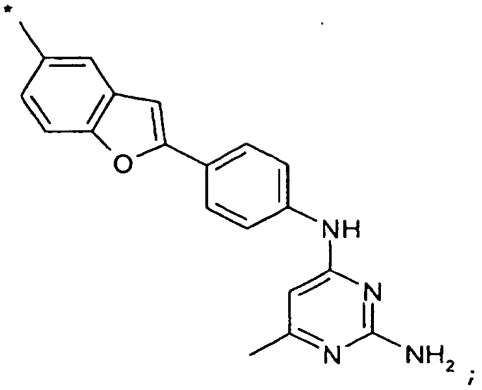
(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N3}R^{N4}$, where n is from 1 to 4 and R^{N3} and R^{N4} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group;

with the provisos that when R^{N1}, R^{N2} and R^2 are H, R^3 is methyl, and X is NH, then R^1 is not:

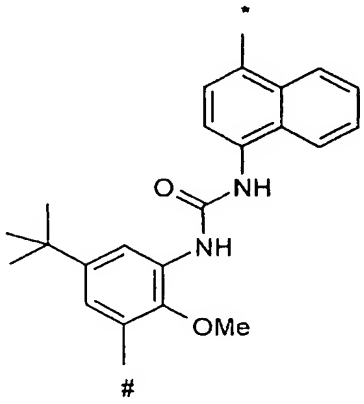


and

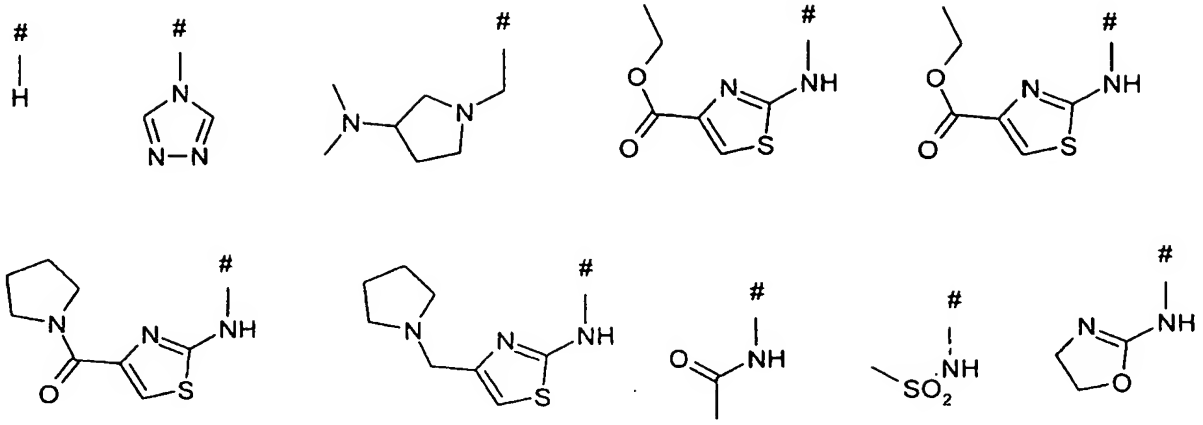


;

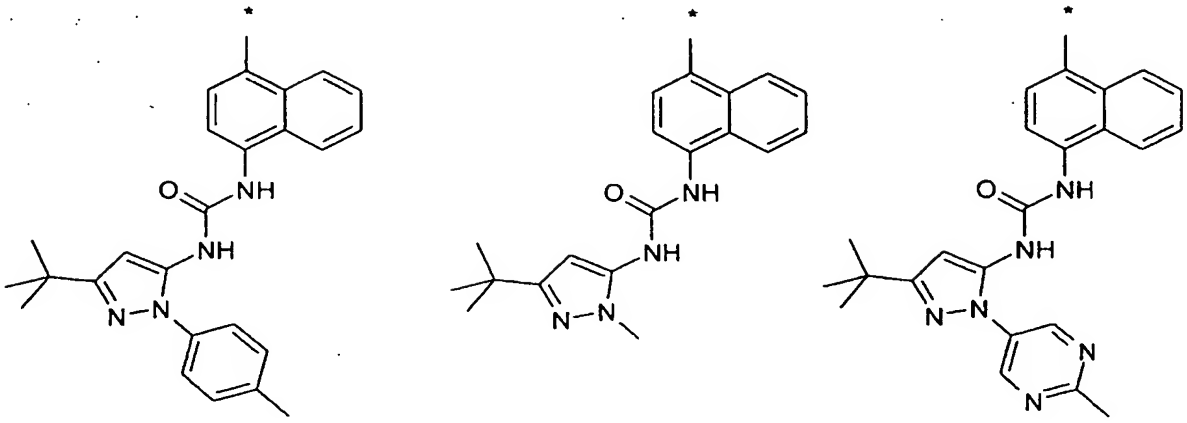
and that when R^2 is H, R^3 is H or Me, R^{N1} and R^{N2} are either (i) independently selected from H, R, R', $(CH_2)_nNR^{N3}R^{N4}$, where n is from 1 to 4 and R^{N3} and R^{N4} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or (ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-6} heterocyclic group; and X is O, then R^1 is not:



wherein # is:



and R^1 is not:



12. The use according to claim 11, wherein R^{N1} and R^{N2} are independently selected from H and R.

13. The use according to claim 12, wherein R^{N1} and R^{N2} are both H.

14. The use according to any one of claims 11 to 13, wherein R^2 is H.

15. The use according to any one of claims 11 to 14, wherein R^3 is methyl.

16. The use according to any one of claims 11 to 15, wherein X is NH.

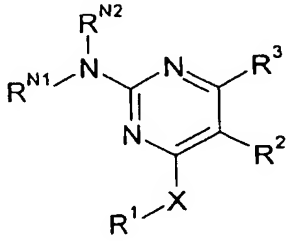
17. The use according to any one of claims 11 to 16, wherein R^1 is an optionally substituted naphthyl group.

18. The use according to any one of claims 11 to 16, wherein R^1 is an optionally substituted biphenyl group.

19. The use according to claim 11, wherein R^1 is a bi-C_{5-7} aryl group optionally substituted with substituent groups independently selected from the group consisting of C_{1-4} alkyl, halo, hydroxy, alkoxy, amino and amido or R^1 is a C_{9-14} aryl group optionally substituted with substituent groups independently selected from the group consisting of C_{1-4} alkyl, halo, hydroxy, alkoxy, cyano, amino and amido.

20. A pharmaceutical composition comprising a compound of formula I as defined in any one of claims 11 to 19, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

21. A compound of formula I:



(I)

or a salt, solvate and chemically protected form thereof, wherein:

X is O or NH;

R^2 and R^3 are independently selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7}

cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;

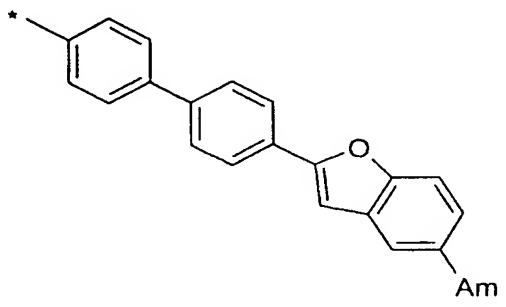
R^1 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N1} and R^{N2} are either:

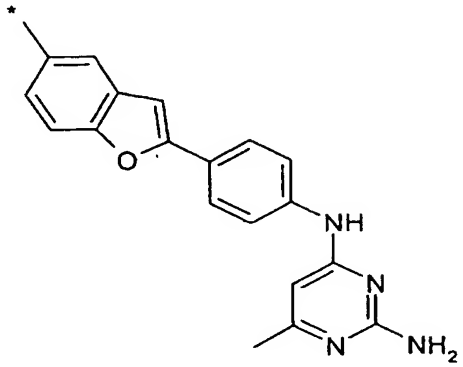
(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N3}R^{N4}$, where n is from 1 to 4 and R^{N3} and R^{N4} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group;

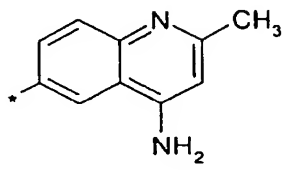
with the provisos that when R^{N1}, R^{N2} and R^2 are H, R^3 is methyl, and X is NH, then R^1 is not:



;

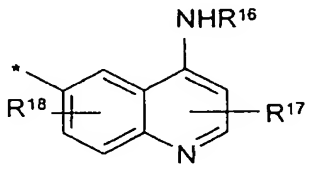


and



;

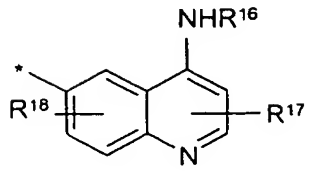
and that when R^{N1} and R^2 are H, R^3 is Me, R^{N2} is H, methyl, or isopropyl, and X is NH, then R^1 is not:



wherein R_{16} is methyl or ethyl and R^{17} and R^{18} are H;

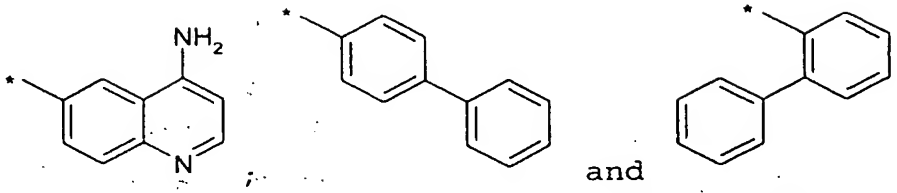
and that when R^{N1}, R^{N2}, R^2 and R^3 are H and X is NH, then R^1

is not:

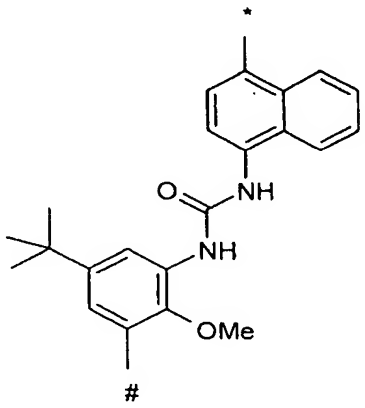


wherein R_{16} is methyl and R^{17} and R^{18} are H,

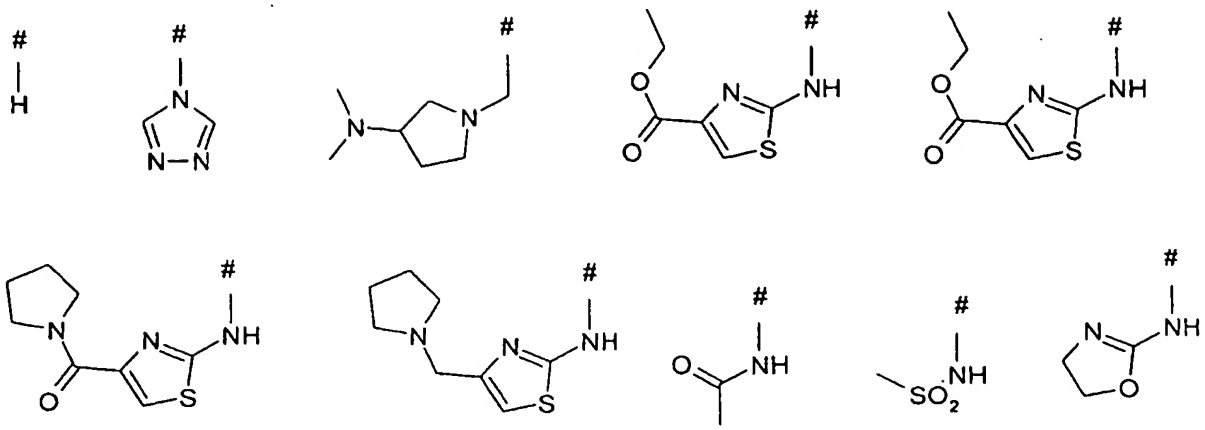
and R^1 is not:



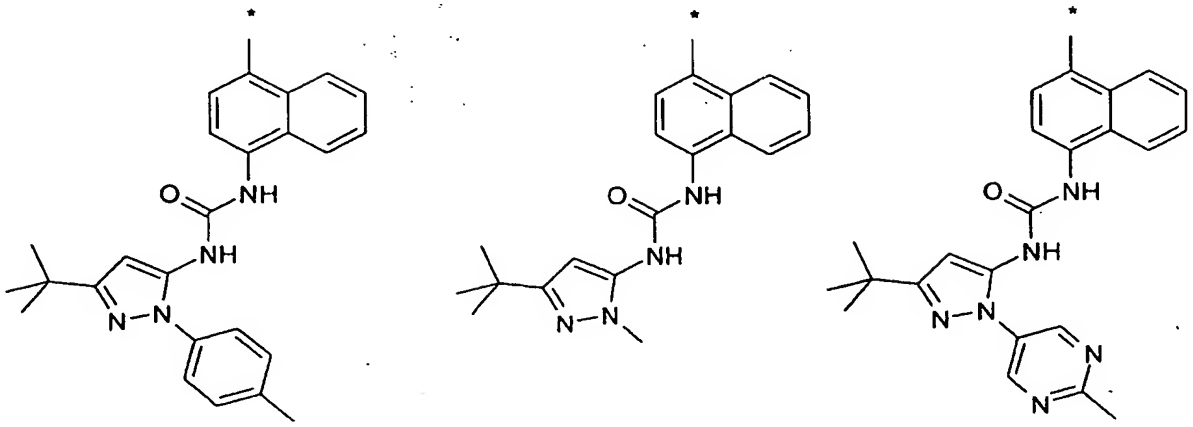
and that when R^2 is H, R^3 is H or Me, R^{N1} and R^{N2} are either (i) independently selected from H, R, R', $(CH_2)_nNR^{N3}R^{N4}$, where n is from 1 to 4 and R^{N3} and R^{N4} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or (ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-6} heterocyclic group; and X is O, then R^1 is not:



wherein # is:

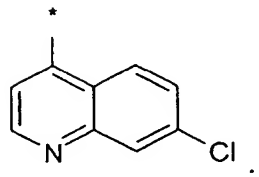


and R^1 is not:



;

and that when when R^{N1}, R^{N2} and R^2 are H, R^3 is methyl, and X is O, then R^1 is not:



22. The compound according to claim 21, wherein R^{N1} and R^{N2} are independently selected from H and R.

23. The compound according to claim 22, wherein R^{N1} and R^{N2} are both H.

24. The compound according to any one of claims 21 to 23, wherein R^2 is H.

35. The compound according to any one of claims 21 to 24, wherein R^3 is methyl.

26. The compound according to any one of claims 21 to 25, wherein X is NH.

27. The compound according to any one of claims 21 to 26, wherein R^1 is an optionally substituted naphthyl group.

28. The compound according to claim 27, wherein the napthyl group is optionally substituted with substituent groups independently selected from the group consisting of C_{1-4} alkyl, halo, hydroxy, alkoxy, cyano, amino and amido.

29. The compound according to any one of claims 21 to 26, wherein R^1 is an optionally substituted biphenyl group.

30. The compound according to claim 21 wherein R^{N1}, R^{N2} and R^2 are H, R^3 is methyl, X is NH and R^1 is a bi-C_{5-7} aryl group optionally substituted with substituent groups independently selected from the group consisting of C_{1-4} alkyl, hydroxy, C_{1-4} alkoxy and NH_2.

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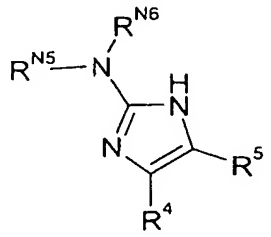
31. The use of a compound of formula II:



(II)

or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT_{2B} receptor,

wherein:

R^5 is selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;

R^4 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N5} and R^{N6} are either:

(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N7}R^{N8}$, where n is from 1 to 4 and R^{N7} and R^{N8} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group.

32. The use according to claim 31, wherein R^{N5} and R^{N6} are independently selected from H, R and C(=O)R, where R is an optionally substituted C_{1-4} alkyl group.

33. The use according to claim 32, wherein at least one of R^{N5} and R^{N6} is H, and the other is selected from H and C(=O)Me.

34. The use according to any one of claims 31 to 33, wherein R^5 is H.

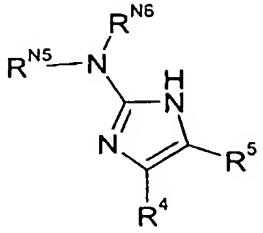
35. The use according to any one of claims 31 to 34, wherein R^4 is preferably a C_{9-14} aryl group or a 3- or 4-C_{5-6} aryl-C_{5-6} aryl group.

36. The use according to claim 35, wherein R^4 is an optionally substituted C_{9-14} carboaryl group.

37. The use according to claim 36, wherein R^4 is an optionally substituted naphthyl group.

38. The use according to any one of claims 31 to 37, wherein the condition alleviated by antagonism of a 5-HT_{2B} receptor is a disorder of the GI tract.

39. The use of a compound of formula II:



(II)

or a pharmaceutically acceptable salt thereof, in a method of therapy, wherein:

R^5 is selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;

R^4 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N5} and R^{N6} are either:

(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N7}R^{N8}$, where n is from 1 to 4 and R^{N7} and R^{N8} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group;

with the proviso that when R^{N5}, R^{N6} and R^5 are H, R^4 is not unsubstituted 1- or 2-naphthyl or unsubstituted 4-phenyl-

phenyl.

40. The use according to claim 39, wherein R^{N5} and R^{N6} are independently selected from H, R and C(=O)R, where R is preferably an optionally substituted C_{1-4} alkyl group.

41. The use according to claim 40, wherein at least one of R^{N5} and R^{N6} is H, and the other is selected from H and C(=O)Me.

42. The use according to any one of claims 39 to 41, wherein R^5 is H.

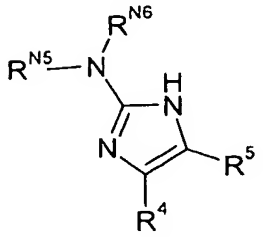
43. The use according to any one of claims 39 to 42, wherein R^4 is preferably an optionally substituted C_{9-14} aryl group or an optionally substituted 3- or 4-C_{5-6} aryl-C_{5-6} aryl group.

44. The use according to claim 43, wherein R^4 is an optionally substituted C_{9-14} carboaryl group.

45. The use according to claim 44, wherein R^4 is an optionally substituted naphthyl group.

46. A pharmaceutical composition comprising a compound of formula II as defined in any one of claims 39 to 45, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

47. A compound of formula II:



(II)

or a salt, solvate and chemically protected form thereof, wherein:

R^5 is selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;

R^4 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N5} and R^{N6} are either:

(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N7}R^{N8}$, where n is from 1 to 4 and R^{N7} and R^{N8} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group;

with the provisos that when R^{N5}, R^{N6} and R^5 are H, R^4 is not unsubstituted 1- or 2-naphthyl or unsubstituted 4-phenyl-phenyl

and that when R^{N6} and R^5 are H, and R^{N5} is acetyl then R^4 is not unsubstituted 2-naphthyl.

48. The compound according to claim 47, wherein R^{N5} and R^{N6} are independently selected from H, R and C(=O)R, where R is preferably an optionally substituted C_{1-4} alkyl group.

49. The compound according to claim 48, wherein at least one of R^{N5} and R^{N6} is H, and the other is selected from H and C(=O)Me.

50. The compound according to any one of claims 47 to 49, wherein R^5 is H.

51. The compound according to any one of claims 47 to 50, wherein R^4 is preferably an optionally substituted C_{9-14} aryl group or an optionally substituted 3- or 4-C_{5-6} aryl-C_{5-6} aryl group.

52. The compound according to claim 51, wherein R^4 is an optionally substituted C_{9-14} carboaryl group.

53. The compound according to claim 52, wherein R^4 is an optionally substituted naphthyl group.

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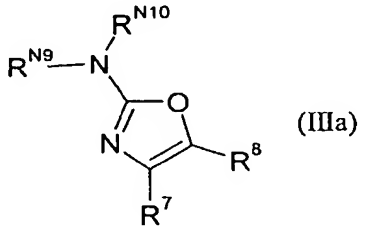
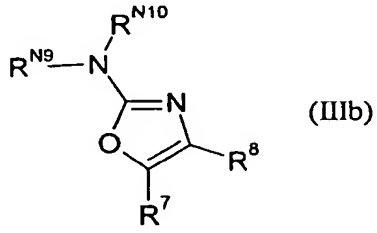
54. The use of a compound of formula IIIa or IIIb:


(IIIa)

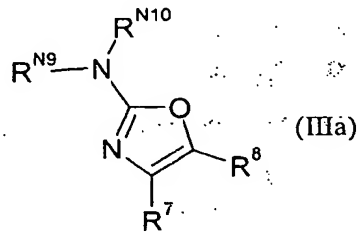

(IIIb)

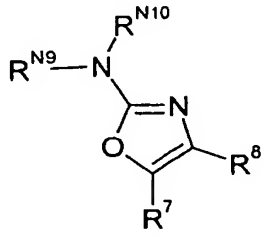
or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT_{2B} receptor, wherein:
R^8 is selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;
R^7 is an optionally substituted bi-C_{5-7} aryl group;
R^{N9} and R^{N10} are either:
(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N11}R^{N12}$, where n is from 1 to 4 and R^{N11} and R^{N12} are independently selected from H and R, where R is optionally

acceptable salt thereof, in a method of therapy.

64. A pharmaceutical composition comprising a compound of formula IIIa or IIIb as defined in any one of claims 54 to 62, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

65. A compound of formula IIIa or IIIb:


(IIIa)


(IIIb)

or a salt, solvate and chemically protected form thereof, wherein:

R^8 is selected from the group consisting of H, and optionally substituted C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4} alkyl, and phenyl-C_{1-4} alkyl;

R^7 is an optionally substituted bi-C_{5-7} aryl group;

R^{N9} and R^{N10} are either:

(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N11}R^{N12}$, where n is from 1 to 4 and R^{N11} and R^{N12} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group;

with the proviso that in formula IIIb, when R^{N9}, R^{N10} and R^8 are H, R^7 is not 4-phenyl-phenyl.

66. The compound according to claim 65, wherein the compound is of formula (IIIb).

67. The compound according to either claim 65 or claim 66, wherein R^8 is selected from H and and optionally substituted C_{1-6} alkyl.

68. The compound according to claim 67, wherein R^8 is H or methyl.

69. The compound according to any one of claims 65 to 68, wherein R^{N9} and R^{N10} are independently selected from H and R.

70. The compound according to claim 69, wherein R is an optionally substituted C_{1-4} alkyl group.

71. The compound according to any one of claims 65 to 70, wherein R^7 is an optionally substituted bi-C_6 aryl group.

72. The compound according to claim 71, wherein R^7 is an optionally substituted bi-phenyl group.

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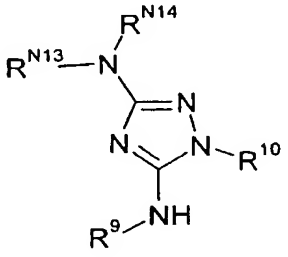
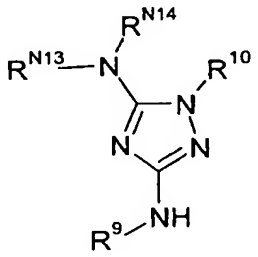
73. A compound of formula IVa or IVb:


(IVa)


(IVb)

or a salt, solvate and chemically protected form thereof, wherein:

R^{10} is selected from the group consisting of H and optionally substituted C_{1-6} alkyl;

R^9 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N13} and R^{N14} are either:

(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N15}R^{N16}$, where n is from 1 to 4 and R^{N15} and R^{N16} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group,

with the proviso that when R^{10}, R^{N13} and R^{N14} are H, R^9 is not an unsubstituted naphthyl group.

74. A compound according to claim 73, wherein the compound is of formula (IVb).

75. The compound according to either claim 73 or claim 74, wherein R^{10} is selected from H and optionally substituted C_{1-6} alkyl.

76. The compound according to claim 75, wherein R^{10} is methyl.

77. The compound according to any one of claims 73 to 76, wherein R^{N13} and R^{N14} are independently selected from H and R.

78. The compound according to claim 77, wherein R is preferably an optionally substituted C_{1-4} alkyl group.

79. The compound according to any one of claims 73 to 78, wherein R^9 is an optionally substituted bi-C_6 aryl group.

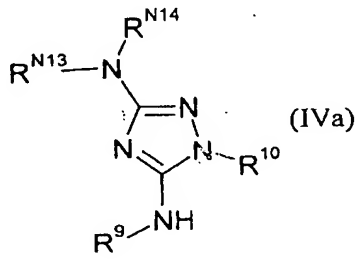
80. The compound according to any one of claims 73 to 79, wherein R^9 is an optionally substituted bi-phenyl group.

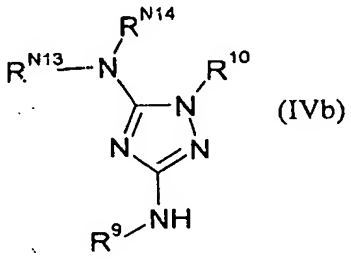
81. The use of a compound of formula IVa or IVb as defined

in any one of claims 73 to 80, or a pharmaceutically acceptable salt thereof in a method of therapy.

82. A pharmaceutical composition comprising a compound of formula IVa or IVb as defined in any one of claims 73 to 80, or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier or diluent.

83. The use of a compound of formula IVa or IVb:


(IVa)


(IVb)

or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of a condition alleviated by antagonism of a 5-HT_{2B} receptor, wherein:

R^{10} is selected from the group consisting of H and optionally substituted C_{1-6} alkyl;

R^9 is an optionally substituted C_{9-14} aryl group or an optionally substituted bi-C_{5-7} aryl group;

R^{N13} and R^{N14} are either:

(i) independently selected from H, R, R', SO_2R, C(=O)R, $(CH_2)_nNR^{N15}R^{N16}$, where n is from 1 to 4 and R^{N15} and R^{N16} are independently selected from H and R, where R is optionally substituted C_{1-4} alkyl, and R' is optionally substituted phenyl-C_{1-4} alkyl, or

(ii) together with the nitrogen atom to which they are attached, form an optionally substituted C_{5-7} heterocyclic group.

84. The use according to claim 83, wherein the condition which can be alleviated by antagonism of a 5-HT_{2B} receptor is a disorder of the GI tract.

85. The use according to either claim 83 or claim 84, wherein the compound is of formula (IVb).

86. The use according to any one of claims 83 to 85, wherein R^{10} is selected from H and optionally substituted C_{1-6} alkyl.

87. The use according to claim 86, wherein R^{10} is methyl.

88. The use according to any one of claims 83 to 87, wherein R^{N13} and R^{N14} are independently selected from H and R.

89. The use according to claim 88, wherein R is preferably an optionally substituted C_{1-4} alkyl group.

90. The use according to any one of claims 83 to 89, wherein R^9 is an optionally substituted bi-C_6 aryl group.

91. The use according to any one of claims 83 to 90, wherein R^9 is an optionally substituted bi-phenyl group.